Perfluoroalkyl Substances (PFAS) Induce Platinum Resistance in Ovarian Cancer by Improving Mitochondrial Membrane Potential and Mitochondrial DNA Copy Number

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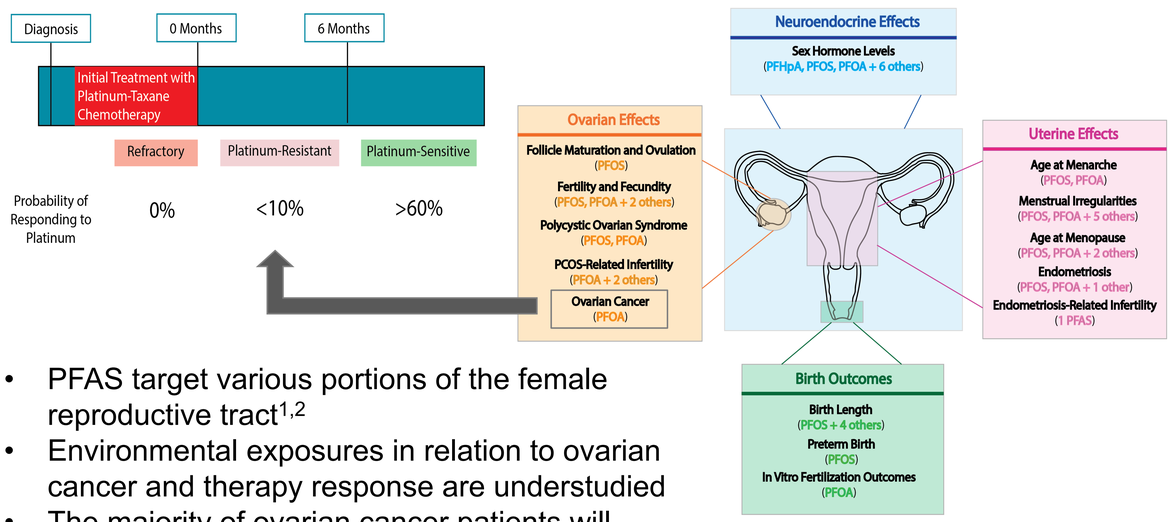
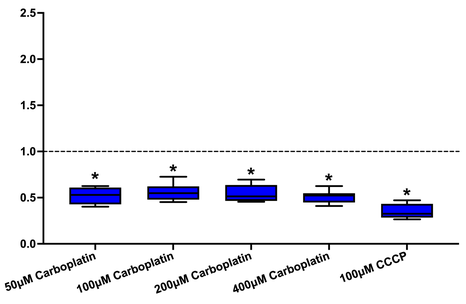
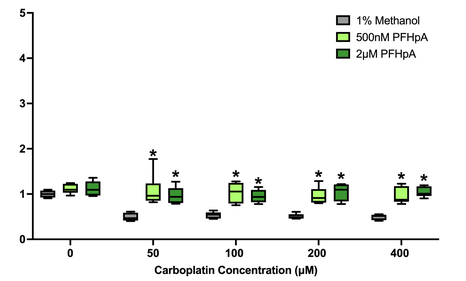
PFAS, Female Reproduction, and Ovarian Cancer



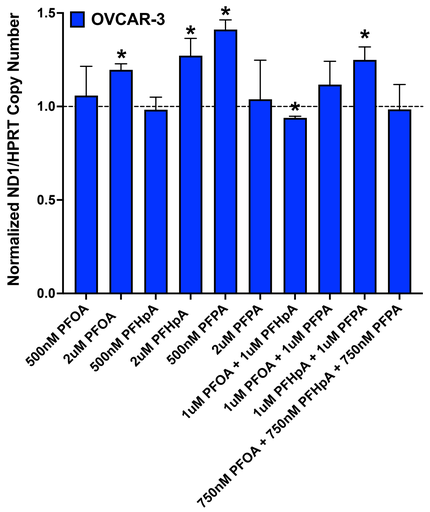
- PFAS target various portions of the female reproductive tract[1,2]
- Environmental exposures in relation to ovarian cancer and therapy response are understudied
- The majority of ovarian cancer patients will develop recurrent, platinum-resistant disease[3]

PFAS Target Mitochondria to Induce Resistance



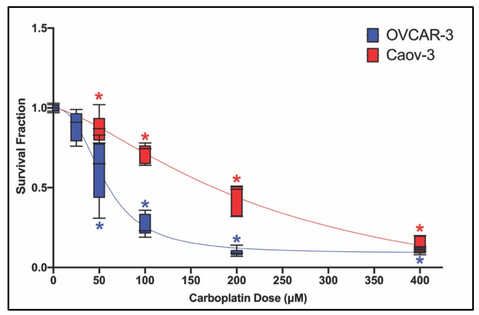


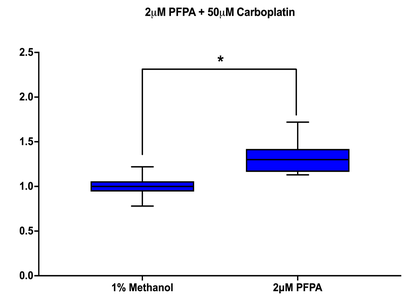
- At baseline, carboplatin decreases OVCAR-3 mitochondrial membrane potential ($\Delta\Psi_m$)[4]
- PFAS that induce platinum resistance also increase $\Delta\Psi_m$, suggestive of improved mitochondrial functioning[4]

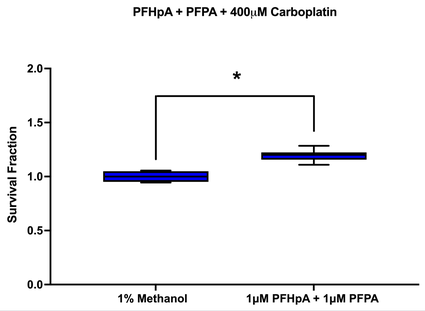


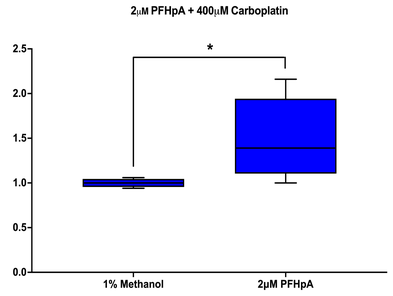
- PFAS exposure leads to alterations, mainly increases, in mtDNA copy number in OVCAR-3 cells

PFAS Induce Platinum Resistance in Ovarian Cancer



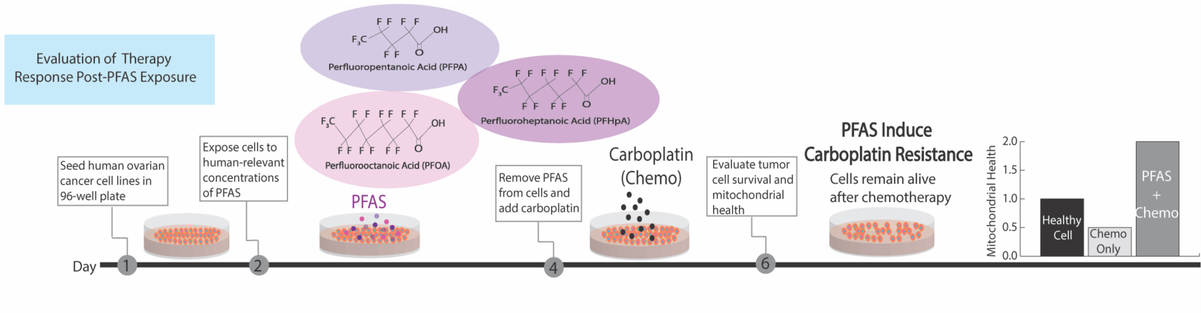






- At baseline, OVCAR-3 cells are responsive to carboplatin[4]
- Select PFAS and PFAS mixtures increase survival fraction in OVCAR-3 cells, indicative of platinum resistance[4]

Summary & Future Directions



SUMMARY

- PFAS induce platinum resistance in ovarian cancer cells
- Mitochondrial membrane potential increases post-PFAS exposure ± carboplatin, but decreases with carboplatin alone
- PFAS exposure increases mtDNA copy number in OVCAR-3 cells

FUTURE DIRECTIONS

- Evaluate bioenergetic pathway activation in ovarian cancer cells post-PFAS exposure
- Chronically expose ovarian cancer cells to PFAS to more adequately match human exposure
- Examine combination chemotherapy (platinum + taxane) in PFAS-exposed cells

References: [1]Rickard *et al*. *Toxicology* (2021).
[2]Ding *et al*. *Human Reproduction Update* (2020).
[3]Foley *et al*. *Oncology* (2013).
[4]Rickard *et al*. *Int. J. Mol. Sci.* (2022).

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